STATEMENT OF FACTS

Counsel for both sides have devoted pages to a description of the "facts" of this case. Briefly, Zonolite Attic Insulation (ZAI) has been manufactured and distributed by the defendants for many years. This is a vermiculite-based product, which contains asbestos. The amount of asbestos is vigorously controverted. The product was marketed as a do-it-yourself insulation product for homeowners that was easy to install. The defendants discontinued sale of the product in the 1980s; however, it continues to function as insulation in many homes in the State of Washington. Prior to commencement of litigation in Washington and several other State Courts and Federal District Courts, in 2000, this product had not been the subject of litigation in an asbestos property damage case.

The plaintiff alleges that ZAI is harmful if disturbed and asbestos fibers become airborne. Due to the age of the product and its use in home construction, it is suggested that many homeowners will be remodeling older homes that are insulated with this product. The airborne fibers, which can result from construction, will be a health hazard to the occupiers of the building as well as any contractors/employees who may work on a project. The plaintiff argues it is appropriate to advise the public of this risk.

DISCUSSION

As noted above, I have already indicated a notice to potential class members of the existence of this litigation is appropriate even though not required when a class is certified under Civil Rule CR 23(b)(2). The question is what should the notice contain?

In order to require the notice contain language that there is a statewide hazard, the plaintiff must show:

> (1) that he or she has a clear legal or equitable right, (2) that he or she has a well-grounded fear of immediate invasion of

> that right, and (3) that the acts complained of are either resulting in or will result in actual and substantial injury to him or her.

King v. Riveland, 125 Wn.2d 500, 515, 886 P.2d 160, 169 (1994)

Has the plaintiff demonstrated there is a statewide hazard, such that court should issue an emergency notice warning citizens of actual and substantial injury that could occur, before a trial on the merits has been conducted? At this time I do not believe the plaintiff has demonstrated an "emergency" which would justify the court sanctioning a notice, and in effect, prejudge the case. There are factual disputes about the quantity of asbestos in vermiculite; whether or not there is any threshold level of exposure, which would not be dangerous; the quantity of asbestos fibers found in the air of the homes tested and the testing protocols used. These are just the type of disputes meant to be resolved by a trial, not a two-day hearing. Therefore, the notice cannot imply that the court has ruled on the merits of the plaintiff's claims.

However, I am also mindful of the ability of the notice to provide information to citizens about governmental efforts to address issues raised in this litigation. As long as the notice is neutral, references to other sources of information about this product may be included as well.

Therefore, the notice to class members should include the following:

- Identify the subject-matter of the litigation
- Identify the court, participants in the litigation and lead counsel
- Identify the criteria for members of the class
- Identify the implications to the class of certification under CR23(b)(2)
- Identify how potential class members should contact plaintiffs' counsel
- Identify how potential class members can find out information about the litigation, i.e. website, newsletter, correspondence etc.
- Identify how potential class members can access other information about the issues in this case, i.e. EPA website, State of Washington Department of Health websites, etc.

There are two suggested notices as exhibits in this case. Neither one is neutral and would not be acceptable to the court. Each party may submit a suggested notice form to the court.

Briefly, the issue of primary jurisdiction has been argued in this case. At this time I do not believe my ruling with respect to the request for preliminary injunction and emergency notice requires that I address the issue. Whether that remains my position depends upon the course of the litigation.

Mr. Scott, please prepare the appropriate order. I have set this matter for presentment on January 19, 2001. A separate hearing should be set to approve the notice form. Please consult my judicial assistant with respect to that hearing.

Dated this 19th day of December, 2000.

KATHLEEN M. O'CONNOR
SUPERIOR COURT JUDGE

Kathleen M. O'Connor
Superior Court Judge

EXHIBIT C

IN THE UNITED STATES BANKRUPTCY COURT
FOR THE DISTRICT OF DELAWARE

IN RE:	)	
	)	
	)	CHAPTER 11
	)	
W. R. GRACE	)	CASE 01-01139JFK

DEPOSITION OF

WILLIAM M. EWING, CIH

May 5, 2003

9:00 a.m

600 Peachtree Street
Bank of America Plaza, Suite 2100
Atlanta, Georgia

Marcia W. Welch, A-172

BROWN Reporting INC.
1740 Peachtree St, N.W.
Atlanta, GA 30309
404-876-8979

A. The indirect method is another method to measure the airborne concentration of asbestos. There have been methods throughout the entire century, the last 100 years, to measure asbestos in different manners but, today, there are different types of microscopy and different preparation methods.

Q. Directing your attention to today, do you know, as a certified industrial hygienist, of any regulatory standards that require indirect preparation of air sampling results?

A. Not for air samples, I do not.

MR. TURKEWITZ: Can you read that back?

(Record was read by the reporter.)

Q. (By Mr Restivo) Do you, sir, agree that the number of asbestos structures found utilizing the indirect method of sample preparation is significantly higher than that prepared by the direct method?

A. Generally, the indirect method provides numbers that are higher than the direct method. Whether they're significantly higher or not depends on the individual samples.

Q. You, in your work, have generally found

Q. (By Mr. Restivo) Well, how many dust samples have you taken in your career, ballpark?

A. Me personally, probably 500 or more.

Q. And after promulgation of the ASTM protocol for dust sampling, when you took dust samples, did you follow that protocol?

A. Almost all the time unless, in some instances, I was maybe comparing different methods or something and made a test for that purpose.

Q. You did dust testing with respect to some residents involved in this case for which you're being deposed today, did you not?

A. Mr. Dawson, that I worked with, took some dust samples, yes.

Q. Okay. Your organization took dust samples?

A. Yes, but I believe Mr. Hatfield may have taken more dust samples than we did.

Q. Okay. And are you prepared to render any opinions with respect to the dust samples taken, whether it was taken by Mr. Dawson, by yourself or by Mr. Hatfield?

A. Yes, I think so.

Q. And were the dust samples that were taken in this case done pursuant to the ASTM protocol, to

your knowledge?

A. The ones that have been analyzed thus far, yes.

Q. Do you agree that that protocol states that it does not describe procedures or techniques required to evaluate the safety or habitability of buildings with asbestos-containing materials?

A. There is some wording to that effect in the standard. I don't have the standard in front of me, so I don't recall the exact words.

Q. You know that concept is in there?

A. Yes.

Q. Do you agree that another concept in that standard is the concept that there is no single direct relationship established between asbestos-containing dust and potential human exposure?

A. Would you say that again?

(Record was read by the reporter.)

THE WITNESS: That sounds like someone's twisted the language that was in there.

Q. (By Mr. Restivo) Okay. I will represent to you that the precise language is, and I quote: "At present, a single direct relationship between asbestos-containing dust and potential human exposure

Q. Now, Mr. Ewing, I'm going to attempt with you to see if I can narrow some issues here. If I'm unsuccessful, I'm unsuccessful.

Would you agree with me that the air sampling results which you reviewed demonstrate that without any disturbance of the material, one does not find any significantly elevated asbestos levels in the air in the homes that you visited?

A. That's correct.

Q. And would you agree with me that with respect to the bulk sampling that was done in these homes, the bulk sampling reports demonstrated less than one percent asbestos in the material?

A. In the homes that I visited, I believe that is correct.

Q. You may have seen other bulk sampling results that are higher than that, but in the homes you visited and the bulk sampling reports you reviewed, it was less than one percent; isn't that correct?

A. In the homes I visited, it was less than one percent. I did review bulk sampling results relating to this case that were more than one percent.

Q. Mr. Ewing, I understand that, but with

A. I'm trying to say no, I'm not going to offer an opinion about that, but I don't want it to come out, no, they don't cause asbestos disease or, yes, they do cause asbestos disease because I don't have an opinion on that because I recognize that it is very controversial and I don't think --

Q. Mr. Ewing, my question --

A. I don't have an opinion to offer.

Q. Thank you. I wasn't asking what your opinion was. I just want you to tell me that's not your area of expertise on that issue?

A. Off the record.

(Discussion ensued off the record.)

Q. (By Mr. Restivo) And, sir, do you have an opinion, to a reasonable degree of scientific certainty, whether cleavage fragments are asbestiform?

A. That gets down to the definition that you want to use for asbestiform. If it's a --

Q. I can rephrase the question or I will withdraw the question.

Mr. Ewing, other than your knowledge and understanding that one counts cleavage fragments and anything else under PCM that has the right dimensions, do you have an opinion, to a reasonable

degree of scientific certainty, whether cleavage fragments are asbestiform?

A. From a geology standpoint, a mineralogist standpoint, I -- my understanding is, from that viewpoint, that they're not considered asbestiform because they don't cleave -- an asbestiform material would cleave along the axis of the fiber or the fiber itself doesn't cleave. It breaks perpendicular to the axis if it breaks. Again, I don't think I will be offering any opinions about it.

Q. Mr. Ewing, I'm going to now turn to your report entitled Zonolite Insulation Exposure Studies. I'm going to probably try to chitchat with you until about 12:30 starting through this report, and then I suggest we break.

What I have, sir, and, counsel, on the table is what I believe to be the package of materials I think the way we got them. I'm not intending to mark that phonebook as an exhibit, and for ease of questioning, I may have shuffled my materials in a little different order so when we're referring to them, I will ask you to be a little patient with me so I can find what it is I need to find, but the package itself is on the table before each of you. I'm not going to make it an exhibit.

both longer than 5 microns and shorter than 5 microns, you didn't precisely follow NIOSH 7402 which only deals with fibers greater than 5 microns for the PCM equivalent calculation?

A. 7402 also -- the PCM equivalent looks at fibers only greater in diameter than .25 micrometers, as well as greater than 5 microns long and an aspect ratio of 3 to 1. Basically, what we wanted to do was look at the 7400 PCM and then look at TEM, all structures, whether they're fibers or clusters or bundles or whatever, greater than .5 but included a 5 micron cutoff, separate it out, so we get reports for both.

Q. And, in addition --

A. Which is really an AHERA analysis.

Q. And, in addition, including fibers with a diameter less than .25?

A. It includes diameters of any fiber size, yes, but not the very short fibers.

Q. No fibers less than .5 in length?

A. Right.

(Exhibit Ewing 2 was marked for identification.)

Q. (By Mr. Restivo) Mr. Ewing, I show you what has been marked Ewing Deposition Exhibit 2. Is

actually there involved in the simulations himself, and so I'm trying to right now address your attention to Dr. Lee's report to see if there is something I need to examine you on.

We'll come back to your possible comment on how the simulations were done. I'm trying to now address your attention to the Lee report.

A. Well, it's unclear to me, then, who's going to testify about their simulations. I didn't see a report from Roger Morris. Perhaps there is one that I didn't see.

Q. Okay. Other than that, and let's put aside whether Dr. Lee is the testifier on that or not, anything else you would express an opinion on with respect to the Dr. Lee report?

A. I don't know what I might be asked about. I do not expect to be asked about how he technically analyzed the samples or whether he followed the -- a particular method in a certain manner. I don't expect to be asked about that. Offhand, I can't think of anything.

Q. Okay. He indicates that surface dust concentrations are not predictors of past or future exposures. Do you expect to comment on that opinion?

A. I think I would -- I think I might be in

agreement, if I'm understanding what he's saying, is that you don't take a surface dust sample and say, based on this dust sample, I know what the average exposure was in this room for the last five years or ten years or what it was a year ago or what it was yesterday.

The same thing with in the future, whether you can take a dust sample and say, based on this dust sample, I can predict what the exposure in this room will be two weeks from now or a year from now. That's not the reason people do dust sampling. I don't recall that statement being there. If it is, I think I would agree with it.

Q. We also have got an expert report, and I think you made reference to this, by Dr. E. B. Ilgren, M.D., who is a medical doctor, pathologist, toxicologist. His report deals with the biological relevance of tremolite cleavage fragments.

Can I safely assume from the testimony you have already given today that you don't expect to express an opinion on the biological relevance of tremolite cleavage fragments?

A. I think you can safely assume that.

Q. And you don't express -- you do not expect to express an opinion on Dr. Ilgren's report?

A. You mean just the number is different?

Q. Yes.

A. Such as you find 5,600 here and over there you find 5,800 or are you asking me --

Q. Material differences?

A. Do I recognize that as being truly different?

Q. No. Do you find material differences when you take dust sampling in the same house in the same room?

A. Sometimes you do and sometimes you don't.

Q. Isn't it true that even when taking duplicate samples at the same place, you have found variations in the dust sampling report?

A. You might.

Q. I understand you might. My question to you is haven't you seen dust sampling reports where you have taken or your organization has taken dust sampling in the exact same spot and received back from the laboratory different results?

A. That has occurred, yes.

Q. Isn't it true that in taking duplicate samples at the same spot, you get variances as much as 100 percent?

A. All the time? No.

Q. No, that you can get variances as much as 100 percent, not necessarily all the time?

A. That's correct.

Q. Is there any requirement under any OSHA regulations mandating the taking of dust samples with respect to asbestos?

A. No, there is not.

Q. Is there any requirement by the EPA with respect to asbestos for the taking of dust samples?

A. It's not required. It's not prohibited in any way. It may be done to help gather additional information.

Q. You would agree with me, as a certified industrial hygienist, that after an abatement, EPA mandates that certain things be done?

A. In school buildings, yes.

Q. You have run abatements, haven't you?

A. Yes.

Q. And you have attempted in those abatements to follow whatever EPA and other regulations you had to follow; isn't that correct?

A. Yes.

Q. And do any of those regulations with respect to abatements mandate dust sampling?

A. No.

EXHIBIT D

Reference Manual on Scientific Evidence

Second Edition

Federal Judicial Center 2000

Preface

Thomas Henry Huxley observed that "science is simply common sense at its best; that is, rigidly accurate in observation and merciless to a fallacy in logic."[1] This second edition of the *Reference Manual on Scientific Evidence* furthers the goal of assisting federal judges in recognizing the characteristics and reasoning of "science" as it is relevant in litigation. The *Reference Manual* is but one part of a series of education and research initiatives undertaken by the Center, in collaboration with other professional organizations, and with support by a grant from the Carnegie Corporation of New York, to aid judges in dealing with these issues. The *Reference Manual* itself responds to a recommendation of the Federal Courts Study Committee that the Federal Judicial Center prepare a manual to assist judges in managing cases involving complex scientific and technical evidence.[2]

The first edition of the *Reference Manual* was published in 1994, at a time of heightened need for judicial awareness of scientific methods and reasoning created by the Supreme Court's decision in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*[3] *Daubert* assigned the trial judge a "gatekeeping responsibility" to make "a preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts in issue."[4] The first edition of the *Reference Manual* has been republished by numerous private publishers and used in a variety of educational programs for federal and state judges, attorneys, and law students. The Center estimates that approximately 100,000 copies have been distributed since its initial publication.

This second edition comes after recent decisions that expand the duties and responsibility of trial courts in cases involving scientific and technical evidence. In *General Electric Co. v. Joiner,*[5] the Supreme Court strengthened the role of the trial courts by deciding that abuse of discretion is the correct standard for an appellate court to apply in reviewing a district court's evidentiary ruling. In a concurring opinion, Justice Breyer urged judges to avail themselves of techniques, such as the use of court-appointed experts, that would assist them in

1. T.H. Huxley, The Crayfish: An Introduction to the Study of Zoology 2 (1880), *quoted in* Stephen Jay Gould, Full House: The Spread of Excellence from Plato to Darwin 8 (1996).

2. Federal Courts Study Comm., Report of the Federal Courts Study Committee 97 (1990). *See also* Carnegie Comm'n on Science, Tech., & Gov't, Science and Technology in Judicial Decision Making: Creating Opportunities and Meeting Challenges 11 (1993) (noting concern over the ability of courts to manage and adjudicate scientific and technical issues).

3. 509 U.S. 579 (1993).

4. *Id.* at 589 n.7, 592–93.

5. 522 U.S. 136, 141–43 (1997).

making determinations about the admissibility of complex scientific or technical evidence.[6] Last year, in *Kumho Tire Co. v. Carmichael*, the Supreme Court determined that the trial judge's gatekeeping obligation under *Daubert* not only applies to scientific evidence but also extends to proffers of "'technical' and 'other specialized' knowledge," the other categories of expertise specified in Federal Rule of Evidence 702.[7] Also, the Supreme Court recently forwarded to Congress proposed amendments to Federal Rules of Evidence 701, 702, and 703 that are intended to codify case law that is based on *Daubert* and its progeny.

This second edition includes new chapters that respond to issues that have emerged since the initial publication. The Introduction by Justice Breyer reviews the role of scientific evidence in litigation and the challenges that trial courts face in considering such evidence. Supreme Court cases subsequent to *Daubert* are summarized in a chapter by Margaret Berger. The philosophy and practice of science are described in a chapter by David Goodstein. New reference guides on medical testimony and engineering will aid judges with the broader scope of review for cases involving nonscientific expert testimony following *Kumho*. Reference guides from the first edition have been updated with new cases and additional material. The Reference Guide on DNA Evidence has been completely revised to take account of the rapidly evolving science in this area. To make room for the new material, essential information from the chapters on court-appointed experts and special masters was condensed and included in the chapter on management of expert evidence.[8]

We continue to caution judges regarding the proper use of the reference guides. They are not intended to instruct judges concerning what evidence should be admissible or to establish minimum standards for acceptable scientific testimony. Rather, the guides can assist judges in identifying the issues most commonly in dispute in these selected areas and in reaching an informed and reasoned assessment concerning the basis of expert evidence. They are designed to facilitate the process of identifying and narrowing issues concerning scientific evidence by outlining for judges the pivotal issues in the areas of science that are often subject to dispute. Citations in the reference guides identify cases in which specific issues were raised; they are examples of other instances in which judges were faced with similar problems. By identifying scientific areas commonly in dispute, the guides should improve the quality of the dialogue between the judges and the parties concerning the basis of expert evidence.

6. *Id.* at 147–50.

7. 119 S. Ct. 1167, 1171 (1999) (quoting Fed. R. Evid. 702).

8. Much of the information in those two chapters is available in Joe S. Cecil & Thomas E. Willging, *Accepting* Daubert*'s Invitation: Defining a Role for Court-Appointed Experts in Assessing Scientific Validity*, 43 Emory L.J. 995 (1994), and Margaret G. Farrell, *Coping with Scientific Evidence: The Use of Special Masters*, 43 Emory L.J. 927 (1994).

This Reference Manual was begun and furthered by two of my predecessors, Judge William W Schwarzer and Judge Rya Zobel. Their work in developing the Center's program on scientific evidence established the foundation for the Center's current initiatives. In developing the *Reference Manual* we benefited greatly from the encouragement and support of David Z. Robinson, former executive director of the Carnegie Commission on Science, Technology, and Government, and Helene Kaplan, chair of the Commission's Task Force on Judicial and Regulatory Decision Making. A number of persons at the Center have been instrumental in developing this second edition of the *Reference Manual.* Joe Cecil and Dean Miletich served as editors of the *Reference Manual.* They profited from the advice and assistance of the following members of the Center's Communications Policy & Design Office: Geoffrey Erwin, Martha Kendall, Kris Markarian, and David Marshall. Rozzie Bell of the Center's Information Services Office offered great assistance in locating much of the source material. Finally, we are grateful to the authors of the chapters for their dedication to the task, and to the peer reviewers of the chapters for their thoughtful suggestions.

FERN M. SMITH
Director, Federal Judicial Center

that if the admissibility test is satisfied, questions of sufficiency remain open for resolution at trial.[80]

2. The role of "general acceptance" and the "intellectual rigor" test

Some early comments predicted that *Kumho* may result in a retreat from *Daubert* and a resurrection of *Frye* because *Kumho*'s flexible approach and abuse-of-discretion standard authorize trial courts to rely on "general acceptance" as the chief screening factor.[81] Such an effect certainly does not seem to have been intended by the Court. The enormous detail with which Justice Breyer described steel-belted radial tires like the Carmichael tire (a sketch is appended to the opinion), the particular characteristics of the ill-fated tire, and Carlson's proposed testimony would all have been unnecessary if the Court's only consideration was "general acceptance." All the Court would have needed to say was that workers in the tire industry did not use Carlson's approach.[82] Although the Court in *Kumho* endorsed an extremely flexible test, it manifested no inclination to return to *Frye*.

This misunderstanding about the role of "general acceptance" may have been enhanced by a passage in which the Court acknowledged the significance of the *Daubert* gatekeeping requirement:

> The objective of that requirement is to ensure the reliability and relevancy of expert testimony. It is to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.[83]

This reference to "the same level of intellectual rigor that characterizes the practice of an expert in the relevant field" is not synonymous with *Frye*'s insistence on "general acceptance" of "the thing from which the deduction is made . . . in the particular field in which it belongs."[84] The difference between these

80. It should also be noted that as of this writing, a proposed amendment to Rule 702 is pending before the Judicial Conference. It would require expert testimony to be "based upon sufficient facts or data." A possible interpretation of this phrase is that the expert's testimony may be excluded if it would not suffice to meet the profferor's burden of persuasion on an issue. The advisory committee notes accompanying the amendment include the following clarification: "The emphasis in the amendment on 'sufficient facts or data' is not intended to authorize a trial court to exclude an expert's testimony on the ground that the court believes one version of the facts and not the other."

81. *See, e.g.*, Michael Hoenig, *New York "Gatekeeping": "Frye" and "Daubert" Coexist*, N.Y. L.J., July 12, 1999, at 3 ("Kumho Tire says the general acceptance standard could be pivotal for trial judges even when non-science or experience-based expert testimony is proffered."); Joseph F. Madonia, Kumho Tire *Steers New Course on Expert-Witness Testimony*, Chi. Daily L. Bull., July 2, 1999, at 5 ("Thus, while superficially appearing to extend *Daubert* to an additional class of expert witnesses, *Kumho Tire* could just as easily end up being an excuse for courts to avoid *Daubert* altogether.").

82. *See supra* note 70 and accompanying text.

83. Kumho Tire Co. v. Carmichael, 119 S. Ct. 1167, 1176 (1999).

84. Frye v. United States, 293 F. 1013, 1014 (D.C. Cir. 1923).

two formulas—which epitomizes the contrast between *Daubert* and *Frye*—becomes apparent if one looks at two Seventh Circuit opinions by Chief Judge Posner in which the "intellectual rigor" standard was first employed.

In *Rosen v. Ciba-Geigy Corp.*,[85] the plaintiff, a heavy smoker with a history of serious heart disease, sued the manufacturer of a nicotine patch that his physician had prescribed in the hope of breaking the plaintiff's cigarette habit. The plaintiff continued to smoke while wearing the patch, despite having been told to stop, and he suffered a heart attack on the third day of wearing the patch.

The district court dismissed the action, after excluding testimony by the plaintiff's cardiologist, Dr. Harry Fozzard, a distinguished department head at the University of Chicago, whose opinion was that the nicotine patch precipitated the heart attack. The court of appeals affirmed the decision. Chief Judge Posner stated that *Daubert*'s object "was to make sure that when scientists testify in court they adhere to the same standards of intellectual rigor that are demanded in their professional work,"[86] and he went on to explain why the district judge had rightly concluded that the cardiologist's proposed testimony did not meet this standard:

> Wearing a nicotine patch for three days, like smoking for three days, is not going to have a significant long-run effect on coronary artery disease; that much is clear. In the long, gradual progression of Rosen's coronary artery disease those three days were a blink of the eye. The patch could have had no significance for Rosen's health, therefore, unless it precipitated his heart attack in June of 1992. That is an entirely different question from whether nicotine, or cigarettes, are bad for one's arteries.
>
> . . . Nowhere in Fozzard's deposition is there an explanation of how a nicotine overdose (for remember that Rosen was smoking at the same time that he was wearing the patch) can precipitate a heart attack, or a reference to a medical or other scientific literature in which such an effect of nicotine is identified and tested. Since Fozzard is a distinguished cardiologist, his conjecture that nicotine can have this effect and may well have had it on Rosen is worthy of careful attention, even though he has not himself done research on the effects of nicotine. But the courtroom is not the place for scientific guesswork, even of the inspired sort. Law lags science; it does not lead it. There may be evidence to back up Fozzard's claim, but none was presented to the district court.[87]

The difference between the "intellectual rigor" standard and the "general acceptance" standard is revealed even more clearly in *Braun v. Lorillard, Inc.*[88] In *Braun*, the plaintiff, who had mesothelioma, sued the manufacturer of his brand of cigarettes on the ground that crocidolite asbestos fibers in the cigarettes' filters had caused his illness. The plaintiff died before trial, and his attorney sought to introduce expert testimony that crocidolite asbestos fibers, the type of asbestos

85. 78 F.3d 316 (7th Cir.), *cert. denied*, 519 U.S. 819 (1996).
86. *Id.* at 318.
87. *Id.* at 319.
88. 84 F.3d 230 (7th Cir.), *cert. denied*, 519 U.S. 992 (1996).

fibers most likely to cause mesothelioma, were found in the decedent's lung tissues. The plaintiff's expert, Schwartz, regularly tested building materials; he had never tested human or animal tissues for the presence of asbestos fibers, or any other substance, before he was hired by the plaintiff's lawyers. The expert was hired after the plaintiff's original experts, who regularly tested human tissue, found nothing. The district court refused to permit testimony at trial concerning the presence of crocidolite asbestos fibers, and the court of appeals affirmed the decision. Chief Judge Posner explained that the Supreme Court in *Daubert* held

> that the opinion evidence of reputable scientists is admissible in evidence in a federal trial even if the particular methods they used in arriving at their opinion are not yet accepted as canonical in their branch of the scientific community. But that is only part of the holding of *Daubert*.[89]

After quoting the "intellectual rigor" test articulated in *Rosen*, Judge Posner stated that "[t]he scientific witness who decides to depart from the canonical methods must have grounds for doing so that are consistent with the methods and usages of his scientific community."[90] That this is a different requirement than the *Frye* test is shown by the sentences in the opinion that immediately follow:

> The district judge did remark at one point that *Daubert* requires that the expert's method be one "customarily relied upon by the relevant scientific community," which is incorrect. But she did not rest her decision to exclude his testimony on that ground. Her ground was that Schwartz had testified "that he really didn't have any knowledge of the methodology that should be employed, and he still doesn't have any information regarding the methodology that should be employed with respect to lung tissue. It seems to me that this witness knows absolutely nothing about analyzing lung tissue and [for?] asbestos fibers."[91]

The court explained further:

> If, therefore, an expert proposes to depart from the generally accepted methodology of his field and embark upon a sea of scientific uncertainty, the court may appropriately insist that he ground his departure in demonstrable and scrupulous adherence to the scientist's creed of meticulous and objective inquiry. To forsake the accepted methods without even inquiring *why* they are the accepted methods—in this case, why specialists in testing human tissues for asbestos fibers have never used the familiar high temperature ashing method—and without even knowing *what* the accepted methods are, strikes us, as it struck Judge Manning, as irresponsible.[92]

It is not enough, therefore, under the "intellectual rigor" test for experts to venture hunches that they would never express or act upon in their everyday

89. *Id.* at 234.
90. *Id.*
91. *Id.*
92. *Id.* at 235.

working lives. Experts must show that their conclusions were reached by methods that are consistent with how their colleagues in the relevant field or discipline would proceed to establish a proposition were they presented with the same facts and issues.

Chief Judge Posner's exposition of the "intellectual rigor" test should not be read as meaning that once a "canonical method" is identified, a court may never inquire further into reliability. Clearly, in *Kumho* the Supreme Court wished to avoid the result sometimes reached under *Frye* when testimony was admitted once experts pointed to a consensus in a narrow field they had themselves established.[93] In the course of discussing the inapplicability of *Daubert* factors in every instance, the Court noted, "[n]or . . . does the presence of *Daubert*'s general acceptance factor help show that an expert's testimony is reliable where the discipline itself lacks reliability, as, for example, do theories grounded in any so-called generally accepted principles of astrology or necromancy."[94] The problem of determining when a discipline lacks reliability is discussed further below.[95]

B. *The Reaffirmation and Extension of* Joiner*'s Abuse-of-Discretion Standard*

1. *The scope of the standard*

In *Kumho*, the Supreme Court extended the *Joiner* abuse-of-discretion standard to all decisions a trial judge makes in ruling on the admissibility of expert testimony, including the procedures it selects to investigate reliability:

> Our opinion in *Joiner* makes clear that a court of appeals is to apply an abuse-of-discretion standard when "it reviews a trial court's decision to admit or exclude expert testimony." That standard applies as much to the trial court's decisions about how to determine reliability as to its ultimate conclusion. Otherwise, the trial judge would lack the discretionary authority needed both to avoid unnecessary "reliability" proceedings in ordinary cases where the reliability of an expert's methods is properly taken for granted, and to require appropriate proceedings in the less usual or more complex cases where cause for questioning the expert's reliability arises.[96]

The adoption of one standard of review for all determinations means that the abuse-of-discretion standard applies even with regard to issues that transcend

93. *See* discussion of the development of voiceprint evidence in Andre A. Moenssens, *Admissibility of Scientific Evidence—An Alternative to the* Frye *Rule*, 25 Wm. & Mary L. Rev. 545, 550 (1984) ("The trend in favor of admitting voiceprints continued until a group of lawyers discovered that, in each case, the same two or three experts had been the proponents who bestowed 'general acceptance' on the technique.").

94. Kumho Tire Co. v. Carmichael, 119 S. Ct. 1167, 1175 (1999).

95. *See infra* text accompanying notes 110–13.

96. *Kumho*, 119 S. Ct. at 1176 (citations omitted).

II. How Have the Data Been Collected?

An analysis is only as good as the data on which it rests.[16] To a large extent, the design of a study determines the quality of the data. Therefore, the proper interpretation of data and their implications begins with an understanding of study design, and different designs help answer different questions. In many cases, statistics are introduced to show causation. Would additional information in a securities prospectus disclosure have caused potential investors to behave in some other way? Does capital punishment deter crime? Do food additives cause cancer? The design of studies intended to prove causation is the first and perhaps the most important topic of this section.

Another issue is the use of sample data to characterize a population: the population is the whole class of units that are of interest; the sample is a set of units chosen for detailed study. Inferences from the part to the whole are justified only when the sample is representative, and that is the second topic of this section.

Finally, it is important to verify the accuracy of the data collection. Errors can arise in the process of making and recording measurements on individual units. This aspect of data quality is the third topic in this section.

A. Is the Study Properly Designed to Investigate Causation?

1. Types of Studies

When causation is at issue, advocates have relied on three major types of information: anecdotal evidence, observational studies, and controlled experiments.[17] As we shall see, anecdotal reports can provide some information, but they are

16. For introductory treatments of data collection, see, e.g., David Freedman et al., Statistics (3d ed. 1998); Darrell Huff, How to Lie with Statistics (1954); David S. Moore, Statistics: Concepts and Controversies (3d ed. 1991); Hans Zeisel, Say It with Figures (6th ed. 1985); and Zeisel & Kaye, *supra* note 1.

17. When relevant studies exist before the commencement of the litigation, it becomes the task of the lawyer and appropriate experts to explain this research to the court. Examples of such "off-the-shelf" research are experiments pinpointing conditions under which eyewitnesses tend to err in identifying criminals and studies of how sex stereotyping affects perceptions of women in the workplace. *See, e.g.*, State v. Chapple, 660 P.2d 1208, 1223–24 (Ariz. 1983) (reversing a conviction for excluding expert testimony about scientific research on eyewitness accuracy); Price Waterhouse v. Hopkins, 490 U.S. 228, 235 (1989). Some psychologists have questioned the applicability of these experiments to litigation. *See, e.g.*, Gerald V. Barrett & Scott B. Morris, *The American Psychological Association's Amicus Curiae Brief in* Price Waterhouse v. Hopkins: *The Values of Science Versus the Values of the Law*, 17 Law & Hum. Behav. 201 (1993). For a rejoinder, see Susan T. Fiske et al., *What Constitutes a Scientific Review?: A Majority Retort to Barrett and Morris*, 17 Law & Hum. Behav. 217 (1993).

If no preexisting studies are available, a case-specific one may be devised. *E.g.*, United States v. Youritan Constr. Co., 370 F. Supp. 643, 647 (N.D. Cal. 1973) (investigating racial discrimination in the rental-housing market by using "testers"—who should differ only in their race—to rent a property),

more useful as a stimulus for further inquiry than as a basis for establishing association. Observational studies can establish that one factor is associated with another, but considerable analysis may be necessary to bridge the gap from association to causation.[18] Controlled experiments are ideal for ascertaining causation, but they can be difficult to undertake.

"Anecdotal evidence" means reports of one kind of event following another. Typically, the reports are obtained haphazardly or selectively, and the logic of "post hoc, ergo propter hoc" does not suffice to demonstrate that the first event causes the second. Consequently, while anecdotal evidence can be suggestive,[19] it can also be quite misleading.[20] For instance, some children who live near power lines develop leukemia; but does exposure to electrical and magnetic fields cause this disease? The anecdotal evidence is not compelling because leukemia also occurs among children who have minimal exposure to such fields.[21] It is necessary to compare disease rates among those who are exposed and those who are not. If exposure causes the disease, the rate should be higher among the exposed, lower among the unexposed. Of course, the two groups may differ in crucial ways other than the exposure. For example, children who live near power

aff'd in part, 509 F.2d 623 (9th Cir. 1975). For a critical review of studies using testers, see James J. Heckman & Peter Siegelman, *The Urban Institute Audit Studies: Their Methods and Findings*, *in* Clear and Convincing Evidence: Measurement of Discrimination in America 187 (Michael Fix & Raymond J. Struyk eds., 1993) (including commentary).

18. For example, smokers have higher rates of lung cancer than nonsmokers; thus smoking and lung cancer are associated.

19. In medicine, evidence from clinical practice is often the starting point for the demonstration of a causal effect. One famous example involves exposure of mothers to German measles during pregnancy, followed by blindness in their babies. N. McAlister Gregg, *Congenital Cataract Following German Measles in the Mother*, 3 Transactions Ophthalmological Soc'y Austl. 35 (1941), *reprinted in* The Challenge of Epidemiology 426 (Carol Buck et al. eds., 1988).

20. Indeed, some courts have suggested that attempts to infer causation from anecdotal reports are inadmissible as unsound methodology under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993). *See, e.g.*, Haggerty v. Upjohn Co., 950 F. Supp. 1160, 1163–64 (S.D. Fla. 1996) (holding that reports to the Food and Drug Administration of "adverse medical events" involving the drug Halcion and "anecdotal case reports appearing in medical literature . . . can be used to generate hypotheses about causation, but not causation conclusions" because "scientifically valid cause and effect determinations depend on controlled clinical trials and epidemiological studies"); Cartwright v. Home Depot U.S.A., Inc., 936 F. Supp. 900, 905 (M.D. Fla. 1996) (excluding an expert's opinion that latex paint caused plaintiff's asthma, in part because "case reports . . . are no substitute for a scientifically designed and conducted inquiry").

21. *See* Committee on the Possible Effects of Electromagnetic Fields on Biologic Sys., National Research Council, Possible Health Effects of Exposure to Residential Electric and Magnetic Fields (1997); Zeisel & Kaye, *supra* note 1, at 66–67. There are serious problems in measuring exposure to electromagnetic fields, and results are somewhat inconsistent from one study to another. For such reasons, the epidemiologic evidence for an effect on health is quite inconclusive. *Id.*; Martha S. Linet et al., *Residential Exposure to Magnetic Fields and Acute Lymphoblastic Leukemia in Children*, 337 New Eng. J. Med. 1 (1997); Edward W. Campion, *Power Lines, Cancer, and Fear*, 337 New Eng. J. Med. 44 (1997) (editorial); Gary Taubes *Magnetic Field-Cancer Link: Will It Rest in Peace?*, 277 Science 29 (1997) (quoting various epidemiologists).

lines could come from poorer families and be exposed to other environmental hazards. These differences could create the appearance of a cause-and-effect relationship, or they can mask a real relationship. Cause-and-effect relationships often are quite subtle, and carefully designed studies are needed to draw valid conclusions.[22]

Typically, a well-designed study will compare outcomes for subjects who are exposed to some factor—the treatment group—and other subjects who are not so exposed—the control group. A distinction must then be made between controlled experiments and observational studies. In a controlled experiment, the investigators decide which subjects are exposed to the factor of interest and which subjects go into the control group. In most observational studies, the subjects themselves choose their exposures. Because of this self-selection, the treatment and control groups are likely to differ with respect to important factors other than the one of primary interest.[23] (These other factors are called confounding variables or lurking variables.[24]) With studies on the health effects of power lines, family background is a possible confounder; so is exposure to other hazards.[25]

22. Here is a classic example from epidemiology. At one time, it was thought that lung cancer was caused by fumes from tarring the roads, because many lung cancer patients lived near roads that had recently been paved. This is anecdotal evidence. But the logic is quite incomplete, because many people without lung cancer were exposed to asphalt fumes. A comparison of rates is needed. Careful study showed that lung cancer patients had similar rates of exposure to tar fumes as other people; the real difference was in exposure to cigarette smoke. Richard Doll & A. Bradford Hill, *A Study of the Aetiology of Carcinoma of the Lung*, 2 Brit. Med. J. 1271 (1952).

23. For present purposes, a variable is a numerical characteristic of units in a study. For instance, in a survey of people, the unit of analysis is the person, and variables might include income (in dollars per year) and educational level (years of schooling completed). In a study of school districts, the unit of analysis is the district, and variables might include average family income of residents and average test scores of students. When investigating a possible cause-and-effect relationship, the variable that characterizes the effect is called the dependent variable, since it may depend on the causes; dependent variables also are called response variables. In contrast, the variables that represent the causes are called independent variables; independent variables also are called factors or explanatory variables.

24. A confounding variable is correlated with the independent variables and with the dependent variable. If the units being studied differ on the independent variables, they are also likely to differ on the confounder. Therefore, the confounder—not the independent variables—could be responsible for differences seen on the dependent variable.

25. Confounding is a problem even in careful epidemiologic studies. For example, women with herpes are more likely to develop cervical cancer than women who have not been exposed to the virus. It was concluded that herpes caused cancer; in other words, the association was thought to be causal. Later research suggests that herpes is only a marker of sexual activity. Women who have had multiple sexual partners are more likely to be exposed not only to herpes but also to human papilloma virus. Certain strains of papilloma virus seem to cause cervical cancer, while herpes does not. Apparently, the association between herpes and cervical cancer is not causal but is due to the effect of other variables. *See* Viral Etiology of Cervical Cancer (Richard Peto & Harald zur Hausen eds., 1986); The Epidemiology of Cervical Cancer and Human Papillomavirus (N. Muñoz et al. eds. 1992). For additional examples and discussion, see Freedman et al., *supra* note 16, at 12–27, 150–52; David Freedman, *From Association to Causation: Some Remarks on the History of Statistics*, 14 Stat. Sci. 243 (1999).

I. Introduction

Epidemiology is the field of public health and medicine that studies the incidence, distribution, and etiology of disease in human populations. The purpose of epidemiology is to better understand disease causation and to prevent disease in groups of individuals. Epidemiology assumes that disease is not distributed randomly in a group of individuals and that identifiable subgroups, including those exposed to certain agents, are at increased risk of contracting particular diseases.[1]

Judges and juries increasingly are presented with epidemiologic evidence as the basis of an expert's opinion on causation.[2] In the courtroom, epidemiologic research findings[3] are offered to establish or dispute whether exposure to an agent[4] caused a harmful effect or disease.[5] Epidemiologic evidence identifies

1. Although epidemiologists may conduct studies of beneficial agents that prevent or cure disease or other medical conditions, this reference guide refers exclusively to outcomes as diseases, because they are the relevant outcomes in most judicial proceedings in which epidemiology is involved.

2. Epidemiologic studies have been well received by courts trying mass tort suits. Well-conducted studies are uniformly admitted. 2 Modern Scientific Evidence: The Law and Science of Expert Testimony § 28-1.1, at 302–03 (David L. Faigman et al. eds., 1997) [hereinafter Modern Scientific Evidence]. It is important to note that often the expert testifying before the court is not the scientist who conducted the study or series of studies. *See, e.g.*, DeLuca v. Merrell Dow Pharms., Inc., 911 F.2d 941, 953 (3d Cir. 1990) (pediatric pharmacologist expert's credentials sufficient pursuant to Fed. R. Evid. 702 to interpret epidemiologic studies and render an opinion based thereon); *cf.* Landrigan v. Celotex Corp., 605 A.2d 1079, 1088 (N.J. 1992) (epidemiologist permitted to testify to both general causation and specific causation); Loudermill v. Dow Chem. Co., 863 F.2d 566, 569 (8th Cir. 1988) (toxicologist permitted to testify that chemical caused decedent's death).

3. An epidemiologic study, which often is published in a medical journal or other scientific journal, is hearsay. An epidemiologic study that is performed by the government, such as one performed by the Centers for Disease Control (CDC), may be admissible based on the hearsay exception for government records contained in Fed. R. Evid. 803(8)(C). *See* Ellis v. International Playtex, Inc., 745 F.2d 292, 300–01 (4th Cir. 1984); Kehm v. Procter & Gamble Co., 580 F. Supp. 890, 899 (N.D. Iowa 1982), *aff'd sub nom.* Kehm v. Procter & Gamble Mfg. Co., 724 F.2d 613 (8th Cir. 1983). A study that is not conducted by the government might qualify for the learned treatise exception to the hearsay rule, Fed. R. Evid. 803(18), or possibly the catchall exceptions, Fed. R. Evid. 803(24) & 804(5). *See Ellis*, 745 F.2d at 305, 306 & n.18.

In any case, an epidemiologic study might be part of the basis of an expert's opinion and need not be independently admissible pursuant to Fed. R. Evid. 703. *See In re* "Agent Orange" Prod. Liab. Litig., 611 F. Supp. 1223, 1240 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988); *cf.* Grassis v. Johns-Manville Corp., 591 A.2d 671, 676 (N.J. Super. Ct. App. Div. 1991) (epidemiologic study offered in evidence to support expert's opinion under New Jersey evidentiary rule equivalent to Fed. R. Evid. 703).

4. We use *agent* to refer to any substance external to the human body that potentially causes disease or other health effects. Thus, drugs, devices, chemicals, radiation, and minerals (e.g., asbestos) are all agents whose toxicity an epidemiologist might explore. A single agent or a number of independent agents may cause disease, or the combined presence of two or more agents may be necessary for the development of the disease. Epidemiologists also conduct studies of individual characteristics, such as blood pressure and diet, which might pose risks, but those studies are rarely of interest in judicial proceedings. Epidemiologists may also conduct studies of drugs and other pharmaceutical products to assess their efficacy and safety.

5. DeLuca v. Merrell Dow Pharms., Inc., 911 F.2d 941, 945–48, 953–59 (3d Cir. 1990) (litigation

agents that are associated with an increased risk of disease in groups of individuals, quantifies the amount of excess disease that is associated with an agent, and provides a profile of the type of individual who is likely to contract a disease after being exposed to an agent. Epidemiology focuses on the question of general causation (i.e., is the agent capable of causing disease?) rather than that of specific causation (i.e., did it cause disease in a particular individual?).[6] For example, in the 1950s Doll and Hill and others published articles about the increased risk of lung cancer in cigarette smokers. Doll and Hill's studies showed that smokers who smoked ten to twenty cigarettes a day had a lung cancer mortality rate that was about ten times higher than that for nonsmokers.[7] These studies identified an association between smoking cigarettes and death from lung cancer, which contributed to the determination that smoking causes lung cancer.

However, it should be emphasized that *an association is not equivalent to causation.*[8] An association identified in an epidemiologic study may or may not be causal.[9] Assessing whether an association is causal requires an understanding of

over morning sickness drug, Bendectin); Cook v. United States, 545 F. Supp. 306, 307–16 (N.D. Cal. 1982) (swine flu vaccine alleged to have caused plaintiff's Guillain-Barré disease); Allen v. United States, 588 F. Supp. 247, 416–25 (D. Utah 1984) (residents near atomic test site claimed exposure to radiation caused leukemia and other cancers), *rev'd on other grounds*, 816 F.2d 1417 (10th Cir. 1987), *cert. denied*, 484 U.S. 1004 (1988); *In re* "Agent Orange" Prod. Liab. Litig., 597 F. Supp. 740, 780–90 (E.D.N.Y. 1984) (Vietnam veterans exposed to Agent Orange and dioxin contaminant brought suit for various diseases and birth defects in their offspring), *aff'd*, 818 F.2d 145 (2d Cir. 1987); Christophersen v. Allied-Signal Corp., 939 F.2d 1106, 1115 (5th Cir. 1991) (cancer alleged to have resulted from exposure to nickel-cadmium fumes), *cert. denied*, 503 U.S. 912 (1992); Kehm v. Procter & Gamble Co., 580 F. Supp. 890, 898–902 (N.D. Iowa 1982) (toxic shock syndrome alleged to result from use of Rely tampons), *aff'd sub nom.* Kehm v. Procter & Gamble Mfg. Co., 724 F.2d 613 (8th Cir. 1983).

6. This terminology and the distinction between general causation and specific causation is widely recognized in court opinions. *See, e.g.*, Kelley v. American Heyer-Schulte Corp., 957 F. Supp. 873, 875–76 (W.D. Tex. 1997) (recognizing the different concepts of general causation and specific causation), *appeal dismissed*, 139 F.3d 899 (5th Cir. 1998); Cavallo v. Star Enter., 892 F. Supp. 756, 771 n.34 (E.D. Va. 1995), *aff'd in part and rev'd in part*, 100 F.3d 1150 (4th Cir. 1996), *cert. denied*, 522 U.S. 1044 (1998); Casey v. Ohio Med. Prods., 877 F. Supp. 1380, 1382 (N.D. Cal. 1995). For a discussion of specific causation, see *infra* § VII.

7. Richard Doll & A. Bradford Hill, *Lung Cancer and Other Causes of Death in Relation to Smoking*, 2 Brit. Med. J. 1071 (1956).

8. *See* Kelley v. American Heyer-Schulte Corp., 957 F. Supp 873, 878 (W.D. Tex. 1997), *appeal dismissed*, 139 F.3d 899 (5th Cir. 1998). Association is more fully discussed *infra* § III. The term is used to describe the relationship between two events (e.g., exposure to a chemical agent and development of disease) that occur more frequently together than one would expect by chance. Association does not necessarily imply a causal effect. Causation is used to describe the association between two events when one event is a necessary link in a chain of events that results in the effect. Of course, alternative causal chains may exist that do not include the agent but that result in the same effect. Epidemiologic methods cannot deductively prove causation; indeed, all empirically based science cannot affirmatively prove a causal relation. *See, e.g.*, Stephan F. Lanes, *The Logic of Causal Inference in Medicine*, *in* Causal Inference 59 (Kenneth J. Rothman ed., 1988). However, epidemiologic evidence can justify an inference that an agent causes a disease. *See infra* § V.

9. *See infra* § IV.

the strengths and weaknesses of the study's design and implementation, as well as a judgment about how the study findings fit with other scientific knowledge. It is important to emphasize that most studies have flaws.[10] Some flaws are inevitable given the limits of technology and resources. In evaluating epidemiologic evidence, the key questions, then, are the extent to which a study's flaws compromise its findings and whether the effect of the flaws can be assessed and taken into account in making inferences.

A final caveat is that employing the results of group-based studies of risk to make a causal determination for an individual plaintiff is beyond the limits of epidemiology. Nevertheless, a substantial body of legal precedent has developed that addresses the use of epidemiologic evidence to prove causation for an individual litigant through probabilistic means, and these cases are discussed later in this reference guide.[11]

The following sections of this reference guide address a number of critical issues that arise in considering the admissibility of, and weight to be accorded to, epidemiologic research findings. Over the past couple of decades, courts frequently have confronted the use of epidemiologic studies as evidence and recognized their utility in proving causation. As the Third Circuit observed in *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*: "The reliability of expert testimony founded on reasoning from epidemiological data is generally a fit subject for judicial notice; epidemiology is a well-established branch of science and medicine, and epidemiological evidence has been accepted in numerous cases."[12]

Three basic issues arise when epidemiology is used in legal disputes and the methodological soundness of a study and its implications for resolution of the question of causation must be assessed:

1. Do the results of an epidemiologic study reveal an association between an agent and disease?
2. What sources of error in the study may have contributed to an inaccurate result?
3. If the agent is associated with disease, is the relationship causal?

Section II explains the different kinds of epidemiologic studies, and section III addresses the meaning of their outcomes. Section IV examines concerns about the methodological validity of a study, including the problem of sampling er-

10. *See In re* Orthopedic Bone Screw Prods. Liab. Litig., MDL No. 1014, 1997 U.S. Dist. LEXIS 6441, at *26–*27 (E.D. Pa. May 5, 1997) (holding that despite potential for several biases in a study that "may . . . render its conclusions inaccurate," the study was sufficiently reliable to be admissible); Joseph L. Gastwirth, *Reference Guide on Survey Research*, 36 Jurimetrics J. 181, 185 (1996) (review essay) ("One can always point to a potential flaw in a statistical analysis.").

11. *See infra* § VII.

12. 911 F.2d 941, 954 (3d Cir. 1990); *see also* Smith v. Ortho Pharm. Corp., 770 F. Supp. 1561, 1571 (N.D. Ga. 1991) (explaining increased reliance of courts on epidemiologic evidence in toxic substances litigation).

ror.[13] Section V discusses general causation, considering whether an agent is capable of causing disease. Section VI deals with methods for combining the results of multiple epidemiologic studies, and the difficulties entailed in extracting a single global measure of risk from multiple studies. Additional legal questions that arise in most toxic substances cases are whether population-based epidemiologic evidence can be used to infer specific causation, and if so, how. Section VII examines issues of specific causation, considering whether an agent caused an individual's disease.

II. What Different Kinds of Epidemiologic Studies Exist?

A. Experimental and Observational Studies of Suspected Toxic Agents

To determine whether an agent is related to the risk of developing a certain disease or an adverse health outcome, we might ideally want to conduct an experimental study in which the subjects would be randomly assigned to one of two groups: one group exposed to the agent of interest and the other not exposed. After a period of time, the study participants in both groups would be evaluated for development of the disease. This type of study, called a randomized trial, clinical trial, or true experiment, is considered the gold standard for determining the relationship of an agent to a disease or health outcome. Such a study design is often used to evaluate new drugs or medical treatments and is the best way to ensure that any observed difference between the two groups in outcome is likely to be the result of exposure to the drug or medical treatment.

Randomization minimizes the likelihood that there are differences in relevant characteristics between those exposed to the agent and those not exposed. Researchers conducting clinical trials attempt to use study designs that are placebo controlled, which means that the group not receiving the agent or treatment is given a placebo, and that use double blinding, which means that neither the participants nor those conducting the study know which group is receiving the agent or treatment and which group is given the placebo. However, ethical and practical constraints limit the use of such experimental methodologies to assessing the value of agents that are thought to be beneficial to human beings.

13. For a more in-depth discussion of the statistical basis of epidemiology, see David H. Kaye & David A. Freedman, Reference Guide on Statistics § II.A, in this manual, and two case studies: Joseph Sanders, *The Bendectin Litigation: A Case Study in the Life Cycle of Mass Torts*, 43 Hastings L.J. 301 (1992); Devra L. Davis et al., *Assessing the Power and Quality of Epidemiologic Studies of Asbestos-Exposed Populations*, 1 Toxicological & Indus. Health 93 (1985). *See also* References on Epidemiology and References on Law and Epidemiology at the end of this reference guide.

When an agent's effects are suspected to be harmful, we cannot knowingly expose people to the agent.[14] Instead of the investigator controlling who is exposed to the agent and who is not, most epidemiologic studies are observational—that is, they "observe" a group of individuals who have been exposed to an agent of interest, such as cigarette smoking or an industrial chemical, and compare them with another group of individuals who have not been so exposed. Thus, the investigator identifies a group of subjects who have been knowingly or unknowingly exposed and compares their rate of disease or death with that of an unexposed group. In contrast to clinical studies, in which potential risk factors can be controlled, epidemiologic investigations generally focus on individuals living in the community, for whom characteristics other than the one of interest, such as diet, exercise, exposure to other environmental agents, and genetic background, may contribute to the risk of developing the disease in question. Since these characteristics cannot be controlled directly by the investigator, the investigator addresses their possible role in the relationship being studied by considering them in the design of the study and in the analysis and interpretation of the study results (see *infra* section IV).

B. The Types of Observational Study Design

Several different types of observational epidemiologic studies can be conducted.[15] Study designs may be chosen because of suitability for investigating the question of interest, timing constraints, resource limitations, or other considerations. An important question that might be asked initially about a given epidemiologic study is whether the study design used was appropriate to the research question.

Most observational studies collect data about both exposure and health outcome in every individual in the study. The two main types of observational studies are cohort studies and case-control studies. A third type of observational study is a cross-sectional study, although cross-sectional studies are rarely useful in identifying toxic agents.[16] A final type of observational study, one in which data about individuals is not gathered, but rather population data about expo-

14. Experimental studies in which human beings are exposed to agents known or thought to be toxic are ethically proscribed. *See* Ethyl Corp. v. United States Envtl. Protection Agency, 541 F.2d 1, 26 (D.C. Cir.), *cert. denied*, 426 U.S. 941 (1976). Experimental studies can be used where the agent under investigation is believed to be beneficial, as is the case in the development and testing of new pharmaceutical drugs. *See, e.g.*, E.R. Squibb & Sons, Inc. v. Stuart Pharms., No. 90-1178, 1990 U.S. Dist. LEXIS 15788 (D.N.J. Oct. 16, 1990); Gordon H. Guyatt, *Using Randomized Trials in Pharmacoepidemiology*, *in* Drug Epidemiology and Post-Marketing Surveillance 59 (Brian L. Strom & Giampaolo Velo eds., 1992). Experimental studies may also be conducted that entail discontinuation of exposure to a harmful agent, such as studies in which smokers are randomly assigned to a variety of smoking-cessation programs or no cessation.

15. Other epidemiologic studies collect data about the group as a whole, rather than about each individual in the group. These group studies are discussed *infra* § II.B.4.

16. *See infra* § II.B.3.

sure and disease are used, is an ecological study.

The difference between cohort studies and case-control studies is that cohort studies measure and compare the incidence of disease in the exposed and unexposed ("control") groups, while case-control studies measure and compare the frequency of exposure in the group with the disease (the "cases") and the group without the disease (the "controls"). Thus, a cohort study takes the exposed status of participants (the independent variable) and examines its effect on incidence of disease (the dependent variable). A case-control study takes the disease status as the independent variable and examines its relationship with exposure, which is the dependent variable. In a case-control study, the rates of exposure in the cases and the rates in the controls are compared, and the odds of having the disease when exposed to a suspected agent can be compared with the odds when not exposed. The critical difference between cohort studies and case-control studies is that cohort studies begin with exposed people and unexposed people, while case-control studies begin with individuals who are selected based on whether they have the disease or do not have the disease and their exposure to the agent in question is measured. The goal of both types of studies is to determine if there is an association between exposure to an agent and a disease, and the strength (magnitude) of that association.

1. Cohort studies

In cohort studies[17] the researcher identifies two groups of individuals: (1) individuals who have been exposed to a substance that is considered a possible cause of a disease and (2) individuals who have not been exposed (see Figure 1).[18] Both groups are followed for a specified length of time, and the proportions of individuals in each group who develop the disease are compared.[19] Thus, as illustrated in Table 1, a researcher would compare the proportion of unexposed individuals (controls) with the disease (b/(a + b)) with the proportion of exposed individuals (cohort) with the disease (d/(c + d)). If the exposure causes

17. Cohort studies also are referred to as prospective studies and follow-up studies.

18. In some studies, there may be several groups, each with a different magnitude of exposure to the agent being studied. Thus, a study of cigarette smokers might include heavy smokers (> 3 packs a day), moderate smokers (1–2 packs a day), and light smokers (< 1 pack a day). *See, e.g.*, Robert A. Rinsky et al., *Benzene and Leukemia: An Epidemiologic Risk Assessment*, 316 New Eng. J. Med. 1044 (1987).

19. Sometimes retrospective cohort studies are conducted, in which the researcher gathers historical data about exposure and disease outcome of the exposed cohort. Harold A. Kahn, An Introduction to Epidemiologic Methods 39–41 (1983). Irving Selikoff, in his seminal study of asbestotic disease in insulation workers, included several hundred workers who had died before he began the study. Selikoff was able to obtain information about exposure from union records and information about disease from hospital and autopsy records. Irving J. Selikoff et al., *The Occurrence of Asbestosis Among Insulation Workers in the United States*, 132 Annals N.Y. Acad. Sci. 139, 143 (1965).

the disease, the researcher would expect a greater proportion of the exposed individuals than of the unexposed individuals to develop the disease.[20]

Figure 1. Design of a Cohort Study

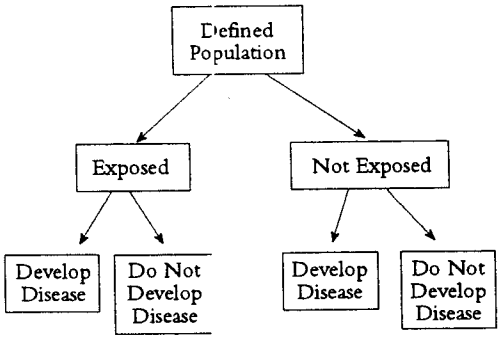


Table 1. Cross-Tabulation of Exposure by Disease Status

	No Disease	Disease
Not Exposed	a	b
Exposed	c	d

One advantage of the cohort study design is that the temporal relationship between exposure and disease can often be established more readily. By tracking the exposed and unexposed groups over time, the researcher can determine the time of disease onset. This temporal relationship is critical to the question of causation, since exposure must precede disease onset if exposure caused the disease.

As an example, in 1950 a cohort study was begun to determine whether uranium miners exposed to radon were at increased risk for lung cancer as compared with nonminers. The study group (also referred to as the exposed cohort) consisted of 3,400 white, underground miners. The control group (which need not be the same size as the exposed cohort) comprised white nonminers from the same geographic area. Members of the exposed cohort were examined ev-

20. Researchers often examine the rate of disease or death in the exposed and control groups. The rate of disease or death entails consideration of the number within a time period. All smokers and nonsmokers will, if followed for 100 years, die. Smokers will die at a greater rate than nonsmokers.

ery three years, and the degree of this cohort's exposure to radon was measured from samples taken in the mines. Ongoing testing for radioactivity and periodic medical monitoring of lungs permitted the researchers to examine whether disease was linked to prior work exposure to radiation and allowed them to discern the relationship between exposure to radiation and disease. Exposure to radiation was associated with the development of lung cancer in uranium miners.[21]

The cohort design is often used in occupational studies such as the one just cited. Since the design is not experimental, and the investigator has no control over what other exposures a subject in the study may have had, an increased risk of disease among the exposed group may be caused by agents other than the exposure of interest. A cohort study of workers in a certain industry that pays below-average wages might find a higher risk of cancer in those workers. This may be because they work in that industry, or, among other reasons, it may be because low-wage groups are exposed to other harmful agents, such as environmental toxins present in higher concentrations in their neighborhoods. In the study design, the researcher must attempt to identify factors other than the exposure that may be responsible for the increased risk of disease. If data are gathered on other possible etiologic factors, the researcher generally uses statistical methods[22] to assess whether a true association exists between working in the industry and cancer. Evaluating whether the association is causal involves additional analysis, as discussed in section V.

2. *Case-control studies*

In case-control studies,[23] the researcher begins with a group of individuals who have a disease (cases) and then selects a group of individuals who do not have the disease (controls). The researcher then compares the groups in terms of past exposures. If a certain exposure is associated with or caused the disease, a higher proportion of past exposure among the cases than among the controls would be expected (see Figure 2).

Thus, for example, in the late 1960s, doctors in Boston were confronted with an unusual incidence of vaginal adenocarcinoma in young female patients. Those patients became the "cases" in a case-control study (because they had the disease in question) and were matched with "controls," who did not have the disease. Controls were selected based on their being born in the same hospitals and at the same time as the cases. The cases and controls were compared for exposure

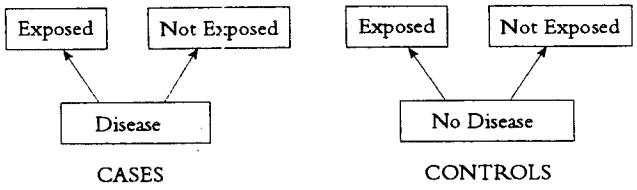
21. This example is based on a study description in Abraham M. Lilienfeld & David E. Lilienfeld, Foundations of Epidemiology 237–39 (2d ed. 1980). The original study is Joseph K. Wagoner et al., *Radiation as the Cause of Lung Cancer Among Uranium Miners*, 273 New Eng. J. Med. 181 (1965).

22. *See* Daniel L. Rubinfeld, Reference Guide on Multiple Regression § II.B, in this manual.

23. Case-control studies are also referred to as retrospective studies, because researchers gather historical information about rates of exposure to an agent in the case and control groups.

to agents that might be responsible, and researchers found maternal ingestion of DES (diethylstilbestrol) in all but one of the cases but none of the controls.[24]

Figure 2. Design of a Case-Control Study



An advantage of the case-control study is that it usually can be completed in less time and with less expense than a cohort study. Case-control studies are also particularly useful in the study of rare diseases, because if a cohort study were conducted, an extremely large group would have to be studied in order to observe the development of a sufficient number of cases for analysis.[25] A number of potential problems with case-control studies are discussed in section IV.B.

3. Cross-sectional studies

A third type of observational study is a cross-sectional study. In this type of study, individuals are interviewed or examined, and the presence of both the exposure of interest and the disease of interest is determined in each individual at a single point in time. Cross-sectional studies determine the presence (prevalence) of both exposure and disease in the subjects and do not determine the development of disease or risk of disease (incidence). Moreover, since both exposure and disease are determined in an individual at the same point in time, it is not possible to establish the temporal relation between exposure and disease—that is, that the exposure preceded the disease, which would be necessary for drawing any causal inference. Thus, a researcher may use a cross-sectional study to determine the connection between a personal characteristic that does not change over time, such as blood type, and existence of a disease, such as aplastic anemia, by examining individuals and determining their blood types and whether they suffer from aplastic anemia. Cross-sectional studies are infrequently used when the exposure of interest is an environmental toxic agent (current smoking status is a poor measure of an individual's history of smoking),

24. *See* Arthur L. Herbst et al., *Adenocarcinoma of the Vagina: Association of Maternal Stilbestrol Therapy with Tumor Appearance*, 284 New Eng. J. Med. 878 (1971).

25. Thus, for example, to detect a doubling of disease caused by exposure to an agent where the incidence of disease is 1 in 100 in the unexposed population would require sample sizes of 3,100 each for a cohort study, but only 177 each for a case-control study. Harold A. Kahn & Christopher T. Sempos, Statistical Methods in Epidemiology 66 (1989).

but these studies can provide valuable leads to further directions for research.[26]

4. Ecological studies

Up to now, we have discussed studies in which data on both exposure and health outcome are obtained for each individual included in the study.[27] In contrast, studies that collect data only about the group as a whole are called ecological studies.[28] In ecological studies, information about individuals is generally not gathered; instead, overall rates of disease or death for different groups are obtained and compared. The objective is to identify some difference between the two groups, such as diet, genetic makeup, or alcohol consumption, that might explain differences in the risk of disease observed in the two groups.[29] Such studies may be useful for identifying associations, but they rarely provide definitive causal answers. The difficulty is illustrated below with an ecological study of the relationship between dietary fat and cancer.

If a researcher were interested in determining whether a high dietary fat intake is associated with breast cancer, he or she could compare different countries in terms of their average fat intakes and their average rates of breast cancer. If a country with a high average fat intake also tends to have a high rate of breast cancer, the finding would suggest an association between dietary fat and breast cancer. However, such a finding would be far from conclusive, because it lacks particularized information about an individual's exposure and disease status (i.e., whether an individual with high fat intake is more likely to have breast cancer).[30] In addition to the lack of information about an individual's intake of fat, the researcher does not know about the individual's exposures to other agents (or other factors, such as a mother's age at first birth) that may also be responsible for the increased risk of breast cancer. This lack of information about each individual's exposure to an agent and disease status detracts from the usefulness of the study and can lead to an erroneous inference about the relationship between fat intake and breast cancer, a problem known as an ecological fallacy. The fallacy is assuming that, on average, the individuals in the study who have

26. For more information (and references) about cross-sectional studies, see Leon Gordis, Epidemiology 137–39 (1996).

27. Some individual studies may be conducted in which all members of a group or community are treated as exposed to an agent of interest (e.g., a contaminated water system) and disease status is determined individually. These studies should be distinguished from ecological studies.

28. In *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545, 1551 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992), the plaintiffs attempted to rely on an excess incidence of cancers in their neighborhood to prove causation. Unfortunately, the court confused the role of epidemiology in proving causation with the issue of the plaintiffs' exposure to the alleged carcinogen and never addressed the evidentiary value of the plaintiffs' evidence of a disease cluster (i.e., an unusually high incidence of a particular disease in a neighborhood or community). *Id.* at 1554.

29. David E. Lilienfeld & Paul D. Stolley, Foundations of Epidemiology 12 (3d ed. 1994).

30. For a discussion of the data on this question and what they might mean, see David Freedman et al., Statistics (3d ed. 1998).

suffered from breast cancer consumed more dietary fat than those who have not suffered from the disease. This assumption may not be true. Nevertheless, the study is useful in that it identifies an area for further research: the fat intake of individuals who have breast cancer as compared with the fat intake of those who do not. Researchers who identify a difference in disease or death in a demographic study may follow up with a study based on gathering data about individuals.

Another epidemiologic approach is to compare disease rates over time and focus on disease rates before and after a point in time when some event of interest took place.[31] For example, thalidomide's teratogenicity (capacity to cause birth defects) was discovered after Dr. Widukind Lenz found a dramatic increase in the incidence of limb reduction birth defects in Germany beginning in 1960. Yet other than with such powerful agents as thalidomide, which increased the incidence of limb reduction defects by several orders of magnitude, these secular-trend studies (also known as time-line studies) are less reliable and less able to detect modest causal effects than the observational studies described above. Other factors that affect the measurement or existence of the disease, such as improved diagnostic techniques and changes in lifestyle or age demographics, may change over time. If those factors can be identified and measured, it may be possible to control for them with statistical methods. Of course, unknown factors cannot be controlled for in these or any other kind of epidemiologic studies.

C. Epidemiologic and Toxicologic Studies

In addition to observational epidemiology, toxicology models based on animal studies (in vivo) may be used to determine toxicity in humans.[32] Animal studies have a number of advantages. They can be conducted as true experiments, and researchers control all aspects of the animals' lives. Thus, they can avoid the problem of confounding,[33] which epidemiology often confronts. Exposure can be carefully controlled and measured. Refusals to participate in a study are not an issue, and loss to follow-up very often is minimal. Ethical limitations are diminished, and animals can be sacrificed and their tissues examined, which may improve the accuracy of disease assessment. Animal studies often provide useful

31. In *Wilson v. Merrell Dow Pharmaceuticals, Inc.*, 893 F.2d 1149, 1152–53 (10th Cir. 1990), the defendant introduced evidence showing total sales of Bendectin and the incidence of birth defects during the 1970–1984 period. In 1983, Bendectin was removed from the market, but the rate of birth defects did not change. The Tenth Circuit affirmed the lower court's ruling that the time-line data were admissible and that the defendant's expert witnesses could rely on them in rendering their opinions.

32. For an in-depth discussion of toxicology, see Bernard D. Goldstein & Mary Sue Henifin, Reference Guide on Toxicology, in this manual.

33. *See infra* § IV.C

information about pathological mechanisms and play a complementary role to epidemiology by assisting researchers in framing hypotheses and in developing study designs for epidemiologic studies.

Animal studies have two significant disadvantages, however. First, animal study results must be extrapolated to another species—human beings—and differences in absorption, metabolism, and other factors may result in interspecies variation in responses. For example, one powerful human teratogen, thalidomide, does not cause birth defects in most rodent species.[34] Similarly, some known teratogens in animals are not believed to be human teratogens. In general, it is often difficult to confirm that an agent known to be toxic in animals is safe for human beings.[35] The second difficulty with inferring human causation from animal studies is that the high doses customarily used in animal studies require consideration of the dose–response relationship and whether a threshold no-effect dose exists.[36] Those matters are almost always fraught with considerable, and currently unresolvable, uncertainty.[37]

Toxicologists also use in vitro methods, in which human or animal tissue or cells are grown in laboratories and exposed to certain substances. The problem with this approach is also extrapolation—whether one can generalize the findings from the artificial setting of tissues in laboratories to whole human beings.[38]

Often toxicologic studies are the only or best available evidence of toxicity. Epidemiologic studies are difficult, time-consuming, and expensive, and consequently they do not exist for a large array of environmental agents. Where both animal toxicology and epidemiologic studies are available, no universal rules exist for how to interpret or reconcile them.[39] Careful assessment of the meth-

34. Phillip Knightley et al., Suffer the Children: The Story of Thalidomide 271–72 (1979).

35. *See* Ian C.T. Nesbit & Nathan J. Karch, Chemical Hazards to Human Reproduction 98–106 (1983); International Agency for Research on Cancer (IARC), Interpretation of Negative Epidemiological Evidence for Carcinogenicity (N.J. Wald & R. Doll eds., 1985).

36. *See infra* § V.C & note 119.

37. *See* General Elec. Co. v. Joiner, 522 U.S. 136, 143–45 (1997) (holding that the district court did not abuse its discretion in excluding expert testimony on causation based on expert's failure to explain how animal studies supported expert's opinion that agent caused disease in humans).

38. For a further discussion of these issues, see Bernard D. Goldstein & Mary Sue Henifin, Reference Guide on Toxicology § III.A, in this manual.

39. *See* IARC, *supra* note 35 (identifying a number of substances and comparing animal toxicology evidence with epidemiologic evidence).

A number of courts have grappled with the role of animal studies in proving causation in a toxic substance case. One line of cases takes a very dim view of their probative value. For example, in *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 313 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990), the court noted the "very limited usefulness of animal studies when confronted with questions of toxicity." A similar view is reflected in *Richardson v. Richardson-Merrell, Inc.*, 857 F.2d 823, 830 (D.C. Cir. 1988), *cert. denied*, 493 U.S. 882 (1989); *Bell v. Swift Adhesives, Inc.*, 804 F. Supp. 1577, 1579–80 (S.D. Ga. 1992); and *Cadurian v. Merrell Dow Pharmaceuticals, Inc.*, 745 F. Supp. 409, 412 (E.D. Mich. 1989). Other courts have been more amenable to the use of animal toxicology in proving causation.

odological validity and power[40] of the epidemiologic evidence must be undertaken, and the quality of the toxicologic studies and the questions of interspecies extrapolation and dose–response relationship must be considered.[41]

Thus, in *Marder v. G.D. Searle & Co.*, 630 F. Supp. 1087, 1094 (D. Md. 1986), *aff'd sub nom.* Wheelahan v. G.D. Searle & Co., 814 F.2d 655 (4th Cir. 1987), the court observed: "There is a range of scientific methods for investigating questions of causation—for example, toxicology and animal studies, clinical research, and epidemiology—which all have distinct advantages and disadvantages." *See also* Villari v. Terminix Int'l, Inc., 692 F. Supp. 568, 571 (E.D. Pa. 1988); Peterson v. Sealed Air Corp., Nos. 86-C3498, 88-C9859 Consol., 1991 U.S. Dist. LEXIS 5333, at *27–*29 (N.D. Ill. Apr. 23, 1991); *cf. In re* Paoli R.R. Yard PCB Litig., 916 F.2d 829, 853–54 (3d Cir. 1990) (questioning the exclusion of animal studies by the lower court), *cert. denied*, 499 U.S. 961 (1991). The Third Circuit in a subsequent opinion in *Paoli* observed:

> [I]n order for animal studies to be admissible to prove causation in humans, there must be good grounds to extrapolate from animals to humans, just as the methodology of the studies must constitute good grounds to reach conclusions about the animals themselves. Thus, the requirement of reliability, or "good grounds," extends to each step in an expert's analysis all the way through the step that connects the work of the expert to the particular case.

In re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 743 (3d Cir. 1994), *cert. denied*, 513 U.S. 1190 (1995); *see also* Cavallo v. Star Enter., 892 F. Supp. 756, 761–63 (E.D. Va. 1995) (courts must examine each of the steps that lead to an expert's opinion), *aff'd in part and rev'd in part*, 100 F.3d 1150 (4th Cir. 1996), *cert. denied*, 522 U.S. 1044 (1998).

One explanation for these conflicting lines of cases may be that when there is a substantial body of epidemiologic evidence that addresses the causal issue, animal toxicology has much less probative value. That was the case, for example, in the Bendectin cases of *Richardson*, *Brock*, and *Cadarian*. Where epidemiologic evidence is not available, animal toxicology may be thought to play a more prominent role in resolving a causal dispute. *See* Michael D. Green, *Expert Witnesses and Sufficiency of Evidence in Toxic Substances Litigation: The Legacy of Agent Orange and Bendectin Litigation*, 86 Nw. U. L. Rev. 643, 680–82 (1992) (arguing that plaintiffs should be required to prove causation by a preponderance of the available evidence); Turpin v. Merrell Dow Pharms., Inc., 959 F.2d 1349, 1359 (6th Cir.), *cert. denied*, 506 U.S. 826 (1992); *In re* Paoli R.R. Yard PCB Litig., No. 86-2229, 1992 U.S. Dist. LEXIS 16287, at *16 (E.D. Pa. Oct. 21, 1992). For another explanation of these cases, see Gerald W. Boston, *A Mass-Exposure Model of Toxic Causation: The Control of Scientific Proof and the Regulatory Experience*, 18 Colum. J. Envtl. L. 181 (1993) (arguing that epidemiologic evidence should be required in mass-exposure cases but not in isolated-exposure cases). *See also* IARC, *supra* note 35; Bernard D. Goldstein & Mary Sue Henifin, Reference Guide on Toxicology § I.F, in this manual. The Supreme Court, in *General Electric Co. v. Joiner*, 522 U.S. 136, 144–45 (1997), suggested that there is not a categorical rule for toxicologic studies, observing, "[W]hether animal studies can ever be a proper foundation for an expert's opinion [is] not the issue. . . . The [animal] studies were so dissimilar to the facts presented in this litigation that it was not an abuse of discretion for the District Court to have rejected the experts' reliance on them."

40. *See infra* § IV.A.3.

41. *See* Ellen F. Heineman & Shelia Hoar Zahm, *The Role of Epidemiology in Hazard Evaluation*, 9 Toxic Substances J. 255, 258–62 (1989).